

# The Hemodynamic Effects of Rapid Intravascular Injection of Protamine Sulphate Following Cardiac Surgery

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Protamine sulphate is routinely used following cardiac surgery to restore the cardiac mechanism to normal by neutralizing the action of heparin. Many toxic side effects such as hypotension, bradycardia, and dyspnea have been described following the intravenous administration of protamine.<sup>1-6</sup>

Measures taken to minimize the unwanted effects of protamine as suggested by the literature include: (1) the slow injection of diluted protamine, (2) the use of a minimal effective dose, and (3) the omission of the neutralization of circulating heparin by protamine sulphate following the cessation of cardio-pulmonary bypass.<sup>4-7</sup> This study describes hemodynamic effects of the rapid injection of non-diluted doses of protamine sulphate in a series of patients following cardiac surgery.

## METHODS AND MATERIALS

Sixty patients were divided into four groups. Group I consisted of those patients in which undiluted doses of protamine sulphate at a ratio of 1.3 to 1 of heparin (300 units per kilogram) was injected within 60 seconds intra-arterially (15 patients). Group II consisted of those patients in which undiluted doses of protamine sulphate was administered as in Group I except that it was administered intravenously (15 patients) following cardiac surgery. Blood volume of Groups I and II was adjusted and maintained to a mean left atrial pressure of at least 14 mm. of mercury. Groups III and IV (30 patients) included patients with hypovolemia (left atrial pressure <5 mm. of mercury and normal arterial pressures). Group III had protamine sulphate injected rapidly (within 60 seconds) intra-arterially (15 patients). Group IV had protamine sulphate injected rapidly (within 60 seconds) intravenously (15 patients). All patients were undergoing some form of cardiac surgery requiring heart-lung bypass. All operations were performed following median sternotomy utilizing aortic root perfusion single venous cannulae drainage via the right atrium, without venting.

Moderate hypothermia, global hypothermic cardioplegia and non-blood prime hemo-dilution with a bubble oxygenator\* was employed. Flow rates of 1.8 to 2.4 liters/per meter<sup>2</sup>/min. were utilized. Following completion of cardiac surgery and after removal of the venous drainage cannulae, protamine sulphate was injected either intravenously via the central venous pressure catheter or intra-arterially via a side arm of the arterial perfusion cannula.<sup>7</sup> (Figure 1) Prior to protamine injection, patients in Groups I and II were transfused with the residual oxygenator blood via the arterial perfusion cannula to maintain a left atrial pressure of at least 14 mm. of mercury. During the period of protamine injection central aortic pressures and left atrial pressures were continuously

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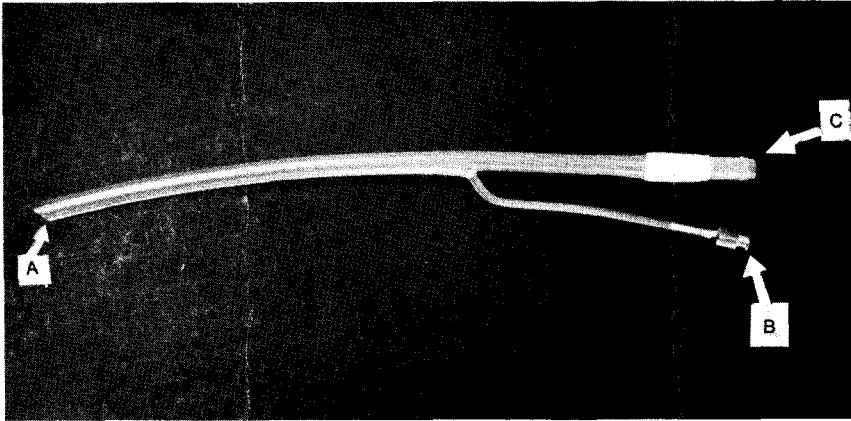


Figure 1. The pressure-monitoring/perfusion cannula, showing: (A) the intravascular portion of the pressure-monitoring port; (B) the extravascular Luer-Lok connector; (C) the connector to the arterial line of the heart-lung machine.

monitored. Intermittent transfusions were used to maintain a left atrial pressure of at least 14 mm. of mercury. In 30 patients with "hypovolemia" (left atrial pressure below 5 mm. of mercury and normal arterial pressure) no transfusions or adjustment in left atrial pressure was made.

Protamine sulphate was also injected rapidly via either the central arterial or central venous lines. Serial measurements in all patients of mean left atrial pressure, central venous pressure, central aortic pressure and peripheral arterial pressure was carried out immediately prior to and 3 minutes following protamine sulphate injection. The mean pressure changes were determined and statistically analyzed by the Student T-tests.

## RESULTS AND DISCUSSION

No significant differences were noted when protamine sulphate was injected intravenously or intra-arterially. In Groups I and II, (left atrial pressure at least 14 mm. of mercury) mean central aortic pressure and left atrial pressure was 120 mm. Hg. and 16 mm. Hg. prior to protamine sulphate and 121 mm. Hg. and 13 mm. Hg. after prota-

TABLE I  
Protamine Sulphate

Group	Pre		3 Min.	Post	
	B.P.	LAP	B.P.	LAP	
I & II 30 pts.	120	15	121	13	
III & IV 30 pts.	115	4	85	0	P < 0.01

mine sulphate. Groups III and IV (left atrial pressure less than 5 mm. of mercury) mean central aortic pressure and left atrial pressure was 115 mm. Hg. and 4 mm. Hg. prior to and 85 mm. Hg. and 0 mm. Hg. after protamine sulphate. (Table I) This hypotensive effect was easily reversed by transfusions to a left atrial pressure of approximately 10-12 mm. of mercury. There were statistically significant differences in arterial pressure between normal and hypovolemic groups of patients, as determined by mean left atrial pressure in response to rapid protamine injection ( $P < 0.01$ ). The authors feel that the hypotensive effect of protamine sulphate can usually be attenuated or eliminated when protamine sulphate is rapidly injected in a hemodynamically stable patient if the left atrial pressure is maintained above 14 mm. of mercury.

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